

In the claims:

Please cancel claims 25-27, 31-34 and 41, without prejudice, and amend claims 1, 13, 28-30, 35, 38, and 46-47 as follows:

(All of the pending claims are reproduced below for the Examiner's convenience).

1. (Three times amended) A method for treating or inhibiting atherosclerosis in a mammal, comprising:
providing an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin and between E-selectin and a ligand of E-selectin; and
administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur, wherein said agent is selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory glycoprotein, and a substance obtained from a snake venom or a plant extract.
2. The method of claim 1 wherein said P-selectin is on a cell.
3. The method of claim 2 wherein said cell is an endothelial cell.
4. The method of claim 2 wherein said cell is a platelet.
5. The method of claim 1 wherein said ligand of P-selectin comprises a carbohydrate.
6. The method of claim 1 wherein said ligand of P-selectin comprises a glycoprotein.
7. The method of claim 1 wherein said ligand of P-selectin is selected from the group consisting of sialyl-Lewis x, sialyl-Lewis a, sialyl-Lewis x-pentasaccharide, polylectosaminoglycan, carbohydrate containing 2, 6 sialic acid, Lewis x 3' -O-sulfate, heparin oligosaccharides, PSGL-1, 160 kD monospecific P-selectin ligand and lysosomal membrane glycoproteins.

8. The method of claim 1 wherein said ligand of P-selectin is on a cell selected from the group consisting of monocytes, neutrophils, eosinophils, CD4+ T cells, CD8+ T cells, and natural killer cells.

9. The method of claim 1 wherein said ligand of P-selectin is on a leukocyte.

10. The method of claim 9 wherein said leukocyte is a neutrophil.

11. The method of claim 9 wherein said leukocyte is a monocyte.

12. The method of claim 1 wherein said P-selectin can bind to said ligand in the absence of said agent.

13. (Twice amended) The method of claim 1 wherein said agent is selected from the group consisting of a soluble form of at least a fragment [portion] of said P-selectin and a soluble form of at least a fragment [portion] of said ligand of P-selectin and mixtures thereof.

19. The method of claim 1 wherein said agent is an inhibitory carbohydrate.

20. The method of claim 19 wherein said inhibitory carbohydrate is selected from the group consisting of sialyl-Lewis x and its analogs, sialyl-Lewis a and its analogs, and carbohydrates containing 2, 6 sialic acid.

23. The method of claim 1 wherein said agent is an inhibitory sulfatide.

24. The method of claim 1 wherein said agent is selected from the group consisting of an analog of said P-selectin and an analog of said ligand of P-selectin and mixtures thereof.

28. (Three times amended) The method of claim 1, wherein said agent inhibits interaction between said P-selectin and said ligand of P-selectin and between said E-selectin and said ligand of E-selectin so as to at least partially inhibit formation of an atherosclerotic fatty streak, or at least partially reverse a formed atherosclerotic fatty streak.

29. (Three times amended) The method of claim 1, wherein said agent inhibits interaction between said P-selectin and said ligand of P-selectin and between said E-selectin and said ligand of E-selectin so as to ~~at least~~ partially inhibit formation of an atherosclerotic intermediate lesion, or at least partially reverse a formed atherosclerotic intermediate lesion.

30. (Three times amended) The method of claim 1, wherein said agent inhibits interaction between said P-selectin and said ligand of P-selectin and between said E-selectin and said ligand of E-selectin so as to at least partially inhibit formation of an atherosclerotic fibrous plaque, or at least partially reverse a formed atherosclerotic fibrous plaque.

35. (Amended) The method of claim 1 wherein said administering occurs prior to or subsequent to formation of an atherosclerotic lesion.

37. The method of claim 1 wherein said mammal is a human.

38. (Three times amended) A therapeutic agent in a dosage form and concentration suitable for treating or inhibiting atherosclerosis in a mammal in need of such treatment, said agent being effective to inhibit interaction between P-selectin and a ligand of P-selectin and between E-selectin and a ligand of E-selectin, wherein said therapeutic agent is selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory glycoprotein, and a substance obtained from a snake venom or a plant extract.

40. The method of claim 19 wherein said inhibitory carbohydrate is a heparin oligosaccharide.

42. The method of claim 19 wherein said agent is administered at a dose of about 0.01 to about 200 mg/kg body weight.

43. The method of claim 23 wherein said agent is administered at a dose of about 100 mg/kg body weight.

44. The method of claim 1 wherein said ligand of P-selectin is on a platelet.

45. The method of claim 1 wherein said agent further inhibits interaction between L-selectin and a ligand of L-selectin.

46. (Amended) A method for treating or inhibiting atherosclerosis in a mammal, comprising:

providing an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin and between L-selectin and a ligand of L-selectin; and

administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur.

47. (Amended) A method for treating or inhibiting atherosclerosis in a mammal, comprising:

providing a first therapeutic agent for inhibiting an interaction between P-selectin and a ligand of P-selectin;

providing a second therapeutic agent for inhibiting interaction between E-selectin and a ligand of E-selectin; and

administering said first agent and said second agent to a mammal in need of such treatment so as to cause such inhibition to occur.

Please add new claims 48-70:

-- 48. The method of claim 1, wherein said agent comprises a soluble form of a P-selectin ligand or a fragment thereof.

49. The method of claim 48, wherein said P-selectin ligand is PSGL-1 or a fragment thereof.

50. The method of claim 1, wherein said agent comprises a chimeric construct between a P-selectin ligand or fragment thereof and another molecule.

51. The method of claim 50, wherein said chimeric construct comprises PSGL-1 or a fragment thereof.

52. The method of claim 1, wherein said agent is an inhibitory glycoprotein.

53. The method of claim 1, wherein said inhibitory glycoprotein contains a sialyl-Lewis x carbohydrate.

54. The method of claim 1, wherein said inhibitory glycoprotein is a 160 kD monospecific P-selectin ligand.

55. The method of claim 1, wherein said agent is administered in sequential exposures over a period of hours, days, weeks, months or years.

56. The method of claim 1, wherein said agent is administered repeatedly, or by a controlled release delivery system.

57. The method of claim 1, wherein said agent is administered in combination with other therapeutic agents.

58. The therapeutic agent of claim 38, wherein said agent comprises a chimeric construct between a P-selectin ligand or fragment thereof and another molecule.

59. The therapeutic agent of claim 58, wherein said chimeric construct comprises PSGL-1 or a fragment thereof.

60. A method for treating or inhibiting atherosclerosis in a mammal, comprising:
providing a chimeric construct between a P-selectin ligand or a fragment thereof and another molecule; and

administering said chimeric construct to a mammal in need of such treatment in an amount sufficient to inhibit an interaction between P-selectin and a ligand of P-selectin.

61. The method of claim 60, wherein said chimeric construct comprises PSGL-1 or a fragment thereof.

62. The method of claim 60, wherein said chimeric construct is administered prior to or subsequent to plaque formation.

63. The method of claim 60, wherein said chimeric construct further inhibits an interaction between E-selectin and a ligand of E-selectin.

64. The method of claim 60, further comprising administering to said mammal a second agent which inhibits an interaction between E-selectin and a ligand of E-selectin, wherein said second agent is selected from the group consisting of an inhibitory protein, an inhibitory peptide, an inhibitory carbohydrate, an inhibitory glycoprotein, and a substance obtained from a snake venom or a plant extract.

65. The method of claim 60, wherein said chimeric construct is administered in sequential exposures over a period of hours, days, weeks, months or years.

66. The method of claim 60, wherein said agent is administered repeatedly, or by a controlled release delivery system.

67. The method of claim 60, wherein said agent is administered in combination with other therapeutic agents.

68. A chimeric construct capable of inhibiting an interaction between P-selectin and a ligand of P-selectin, said chimeric construct comprising a P-selectin ligand or a fragment thereof and another molecule.

69. The chimeric construct of claim 68, wherein said P-selectin ligand is PSGL-1 or a fragment thereof.

70. A method for treating or inhibiting atherosclerosis in a mammal, comprising: providing an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin; and

administering said agent to a mammal in need of such treatment so as to cause such inhibition to occur, wherein said agent is a mimetic of P-selectin or the ligand.--

Remarks

Pending Claims

Claims 25-27, 31-34 and 41 have been canceled, and claims 1, 13, 28-30, 35, 38, and 46-47 have been amended, without prejudice. Claims 48-70 have been added. Upon entry of this amendment, claims 1-13, 19-20, 23-24, 28-30, 35, 37-38, 40, 42-70 will be pending. No new subject matter has been added, and the new claims should not necessitate an additional search.